Complete Summary

GUIDELINE TITLE

Prevention of Hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP).

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1999 Oct 1;48(RR-12):1-37. [161 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Hepatitis A

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Plans
Nurses
Patients
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To present recommendations representing the next phase of the hepatitis A immunization strategy, updated from 1996 (MMWR 1996 Dec 27; 45(RR-15):1-30)
- To present previous recommendations regarding the vaccination of persons in groups at increased risk for hepatitis A or its adverse consequences and recommendations regarding the use of immune globulin (IG) for protection against hepatitis A

TARGET POPULATION

Individuals and populations at increased risk of hepatitis A virus (HAV) disease:

- For preexposure protection with HAV vaccination: Persons greater than or equal to 2 years old at increased risk or HAV infection or the adverse consequences of infection. Risk groups include travelers to endemic areas, persons with chronic liver disease, children in communities that have high or intermediate rates of hepatitis A and periodic hepatitis A outbreaks; men who have sex with men; illegal-drug users; persons who have occupational risk for infection (i.e., who work with HAV-infected primates or who work with HAV in a research laboratory setting).
- For postexposure prophylaxis with immune globulin: All persons who have been exposed to HAV who have not previously been administered hepatitis A vaccine.

INTERVENTIONS AND PRACTICES CONSIDERED

- Preexposure protection against hepatitis A virus (HAV) infection with hepatitis A vaccines, HAVRIX or VAQTA
- Routine vaccination statewide of children living in states with high rates of hepatitis A
- Postexposure prophylaxis against HAV infection with immune globulin

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

I. Preexposure Protection Against Hepatitis A Virus Infection

Hepatitis A vaccination provides preexposure protection from hepatitis A virus (HAV) infection in children and adults. Hepatitis A vaccination is recommended for persons who are at increased risk for infection and for any person wishing to obtain immunity.

A. Children Who Should Be Routinely Vaccinated or Considered for Vaccination

Children living in areas where rates of hepatitis A are at least twice the national average should be routinely vaccinated. These children include:

- Children who live in states where the average annual hepatitis A rate during 1987-1997 was greater than or equal to 20 cases per 100,000 population (i.e., approximately twice the national average).
- Children who live in counties or communities where the average annual hepatitis A rate during 1987-1997 was greater than or equal to 20 cases per 100,000 population.

Children living in areas where rates of hepatitis A are greater than the national average but lower than twice the national average should be considered for routine vaccination. These children include:

- Children who live in states where the average annual rate of hepatitis A during 1987-1997 was greater than or equal to 10 cases per 100,000 population (i.e., approximately the national average) but less than 20 cases per 100,000 population.
- Children who live in counties or communities where the average annual rate of hepatitis A during 1987-1997 was greater than or equal to 10 cases per 100,000 population but less than 20 cases per 100,000 population.

For children living in states with rates of hepatitis A that are greater than or equal to twice the national average for 1987-1997, routine vaccination statewide is recommended. For children living in states where disease incidence is lower than twice the national average, the decision of whether to adopt a statewide or community-based (e.g., county, city, or town) vaccination strategy should include considerations such as feasibility of implementation, the extent to which areas with elevated rates cluster, and whether the strategy is likely to lower overall disease incidence in the state.

Determination of age groups recommended for vaccination should take into consideration community disease patterns. In communities with

high rates of hepatitis A (e.g., American Indian reservations, Alaskan Native villages), routine vaccination of children beginning at greater than or equal to 2 years of age and catch-up vaccination of preschool children should receive highest priority, as previously recommended. In addition, to more effectively prevent epidemics of hepatitis A in these communities, vaccination of previously unvaccinated older children (e.g., up to 10-15 years of age) continues to be recommended. Prevaccination serologic testing is not indicated for vaccination of previously unvaccinated children in this setting.

In other areas where routine childhood vaccination is recommended, possible strategies include vaccinating one or more single-age cohorts of children or adolescents (e.g., children at the age of entry into preschool, elementary school, and/or middle school), vaccination of children and adolescents in selected settings (e.g., day care) or vaccination of children and adolescents over a wide range of ages in a variety of settings, such as when they seek health care for other purposes.

B. Populations at Increased Risk For HAV Infection Who Should be Routinely Vaccinated

Persons traveling to or working in countries that have high or intermediate endemicity of infection. All susceptible persons traveling to or working in countries that have high or intermediate HAV endemicity should be vaccinated or receive immune globulin (IG) before departure. Hepatitis A vaccination at the age-appropriate dose is preferred for children, adolescents, and adults who plan frequent travel or who reside for long periods in a high-risk area. IG is recommended for travelers less than 2 years of age because the vaccine is currently not licensed for use in this age group. Prevaccination testing should be considered for older travelers or for younger persons in certain population groups.

Travelers to Canada, western Europe, Japan, Australia, or New Zealand are at no greater risk for infection than in the United States.

Travelers who are administered vaccine can be assumed to be protected by 4 weeks after receiving the first vaccine dose and therefore should receive this dose at least 4 weeks before departure. Although according to both vaccines' licensure information, the first dose can be given at least 2 weeks before departure, available data suggest that 40% to 45% of vaccinated persons might lack neutralizing antibody at 14 days after receiving the first dose. No data are currently available regarding the risk for hepatitis A among persons vaccinated 2 to 4 weeks before departure. Because protection might not be complete until 4 weeks after vaccination, persons traveling to a high-risk area less than 4 weeks after the initial dose also should be administered IG (0.02 mL/kg), but at a different anatomic injection site. A second vaccine dose administered according to the recommended schedule provided in the guideline document is necessary for long-term protection.

Travelers who are allergic to a vaccine component or who elect not to receive vaccine should receive a single dose of IG (0.02 mL/kg), which provides effective protection against hepatitis A for up to 3 months. Travelers whose travel period exceeds 2 months should be administered IG at 0.06 mL/kg; administration must be repeated if the travel period exceeds 5 months.

Men who have sex with men. Sexually active men who have sex with men (both adolescents and adults) should be vaccinated. Prevaccination testing is not indicated for the vaccination of adolescents and young adults in this group but might be warranted for older adults.

Illegal-drug users. Vaccination is recommended for users of injecting and non-injecting illegal drugs. Prevaccination testing is not indicated for the vaccination of adolescent users of illegal drugs but might be warranted for adults.

Persons who have occupational risk for infection. Persons who work with HAV-infected primates or with HAV in a research laboratory setting should be vaccinated. Studies conducted to date among U.S. workers exposed to raw sewage do not indicate a significantly increased risk for HAV infection. No other groups have been shown to be at increased risk for HAV infection because of occupational exposure.

Persons who have clotting-factor disorders. Susceptible persons who are administered clotting-factor concentrates, especially solvent-detergent-treated preparations, should be administered hepatitis A vaccine.

C. Vaccination of Persons Who Have Chronic Liver Disease

Susceptible persons who have chronic liver disease should be vaccinated. Available data do not indicate a need for routine vaccination of persons with chronic hepatitis B virus or hepatitis C virus infections without evidence of chronic liver disease. Susceptible persons who either are awaiting or have received liver transplants also should be vaccinated.

D. Hepatitis A Vaccination During Outbreaks

Vaccination for outbreak-control should take into consideration the characteristics of hepatitis A epidemiology in the community and existing hepatitis A vaccination programs.

Outbreaks in communities with high rates of hepatitis A. If routine vaccination programs have not achieved at least 70% vaccination coverage of preschool and school-age children, intensified vaccination efforts among preschool children and an accelerated vaccination program for school-age children should be implemented to

achieve these coverage levels. The upper age for vaccination of older, previously unvaccinated children should be determined by using age-specific rates of hepatitis A (or seroprevalence data, if available) but will usually be 10-15 years of age. To prevent future outbreaks, ongoing vaccination of young children should be maintained once the outbreak has subsided.

Outbreaks in communities with intermediate rates of hepatitis A. Routine vaccination of children is recommended for most of these communities and implementation of these programs will eventually prevent outbreaks. If routine childhood vaccination has not been implemented, this should be initiated as recommended.

Accelerated vaccination can be considered as an additional measure to control these outbreaks. These communities often are located in large cities or counties; thus, widespread vaccination might not be feasible. Because outbreaks in these communities often involve both children and adults and might include adults in groups at increased risk for infection (e.g., illegal-drug users, men who have sex with men), local surveillance and epidemiologic data should be used to define populations (e.g., age groups or risk groups) or areas (e.g., census tracts) within the community that have the highest rates of disease. Factors to consider in deciding whether to initiate an outbreak-control vaccination program include the feasibility of rapidly vaccinating the target population of children, adolescents, or young adults, and program cost. Vaccination programs to control outbreaks occurring primarily among adults in identified risk groups (i.e., men who have sex with men, injecting-drug users) have been difficult to implement. Therefore, efforts to control ongoing hepatitis A outbreaks among adults in these groups also should involve initiating and sustaining routine vaccination of these persons to prevent future outbreaks. Because the results of vaccination programs to control hepatitis A outbreaks in communities that have intermediate rates of disease have been variable, evaluation of the effectiveness should be an essential element of programs in these settings. In all such communities, ongoing vaccination of children should be sustained to maintain high levels of immunity and prevent future epidemics.

Outbreaks in communities with low rates of hepatitis A. Community-wide outbreaks are uncommon in communities with low rates of hepatitis A. If outbreaks occur, the response should be based on an examination of the epidemiologic characteristics of the outbreak. Vaccination programs to control outbreaks occurring primarily among adults in identified risk groups (i.e., men who have sex with men, injecting-drug users) have been difficult to implement. Therefore, efforts to control and prevent hepatitis A outbreaks among adults in these groups primarily should be focused on initiating and sustaining routine vaccination of these persons. If outbreaks involving children occur, implementing programs similar to those recommended for intermediate rate communities can be considered, including ongoing routine vaccination of children.

Outbreaks in other settings. The frequency of outbreaks in day care centers, hospitals, institutions (e.g., institutions for the developmentally disabled, prisons), and schools is not high enough to warrant routine hepatitis A vaccination of persons specifically because they are in these settings, and few data exist regarding the role of hepatitis A vaccine in controlling outbreaks in these settings. When outbreaks are recognized in day care centers, aggressive use of IG is effective in limiting transmission to employees and families of attendees (see below). When outbreaks occur in hospitals, institutions, and schools, use of IG for persons in close contact with infected patients or students is recommended (see below). In areas where routine childhood vaccination is recommended, previously unvaccinated children receiving postexposure prophylaxis with IG could also receive hepatitis A vaccine.

Persons who work as food handlers can contract hepatitis A and potentially transmit HAV to others. To decrease the frequency of evaluations of food handlers with hepatitis A and the need for postexposure prophylaxis of patrons, consideration may be given to vaccination of employees who work in areas where state and local health authorities or private employers determine that such vaccination is cost-effective.

II. Postexposure Prophylaxis With Immune Globulin

Persons who have been recently exposed to HAV and who have not previously been administered hepatitis A vaccine should be administered a single IM dose of IG (0.02 mL/kg) as soon as possible, but not greater than 2 weeks after the last exposure. Persons who have been administered one dose of hepatitis A vaccine at least 1 month before exposure to HAV do not need IG.

Because hepatitis A cannot be reliably diagnosed on clinical presentation alone, serologic confirmation of HAV infection in index patients by IgM anti-HAV testing is recommended before postexposure treatment of contacts. Screening of contacts for immunity before giving IG is not recommended because screening is likely to be more costly than IG and would delay its administration.

IG should be administered to previously unvaccinated persons in the following situations. If hepatitis A vaccine is recommended for a person being given IG, it can be administered simultaneously with IG at a separate anatomic injection site. The use of hepatitis A vaccine alone is not recommended for postexposure prophylaxis.

Close personal contact. IG should be administered to all previously unvaccinated household and sexual contacts of persons who have serologically confirmed hepatitis A. In addition, persons who have shared illegal drugs with a person who has serologically confirmed hepatitis A should receive IG and hepatitis A vaccine. Consideration should also be given to providing IG to persons with other types of ongoing, close personal contact (e.g., regular babysitting).

Day care centers. IG should be administered to all previously unvaccinated staff and attendees of day care centers or homes if a) one or more cases of hepatitis A are recognized in children or employees or b) cases are recognized in two or more households of center attendees. In centers that do not provide care to children who wear diapers, IG need be given only to classroom contacts of an index case-patient. When an outbreak occurs (i.e., hepatitis cases in three or more families), IG also should be considered for members of households that have children (center attendees) in diapers. In those communities where routine vaccination is recommended, hepatitis A vaccine can be administered at the same time as IG for children receiving postexposure prophylaxis in day care centers.

Common-source exposure. If a food handler is diagnosed with hepatitis A, IG should be administered to other food handlers at the same establishment. Because common-source transmission to patrons is unlikely, IG administration to patrons is usually not recommended but can be considered if a) during the time when the food handler was likely to be infectious, the food handler both directly handled uncooked foods or foods after cooking and had diarrhea or poor hygienic practices; and b) patrons can be identified and treated within 2 weeks after the exposure. In settings where repeated exposures to HAV might have occurred (e.g., institutional cafeterias), stronger consideration of IG use might be warranted. In the event of a common-source outbreak, IG should not be administered to exposed persons after cases have begun to occur because the 2-week period during which IG is effective will have been exceeded.

Schools, hospitals, and work settings. IG is not routinely indicated when a single case occurs in an elementary or secondary school, an office, or in other work settings, and the source of infection is outside the school or work setting. Similarly, when a person who has hepatitis A is admitted to a hospital, staff should not routinely be administered IG; instead, careful hygienic practices should be emphasized. IG should be administered to persons who have close contact with index patients if an epidemiologic investigation indicates HAV transmission has occurred among students in a school or among patients or between patients and staff in a hospital.

III. Future Considerations

Implementation of these recommendations should significantly lower the incidence of hepatitis A in the United States. When this occurs, the opportunity will be present to eliminate HAV transmission. However, to achieve this goal, children throughout the United States will need to be vaccinated against hepatitis A. This effort would be facilitated by the availability of a vaccine formulation or schedule for use in infants or children in the second year of life and combination vaccines that include hepatitis A vaccine. In the interim, a number of issues should be addressed through clinical trials and other studies:

- Further evaluation of vaccine safety with increased use of hepatitis A vaccine;

- Determining vaccine doses or schedules to overcome the reduced immune response among infants who have passively acquired maternal anti-HAV;
- Developing vaccines that combine HAV antigen with other antigens to more readily integrate hepatitis A vaccine into childhood vaccination schedules;
- Evaluating the cost-effectiveness of integrating hepatitis A vaccine into the routine childhood vaccination schedule;
- Determining whether hepatitis A vaccine will provide an adequate level of postexposure protection against hepatitis A

Determining the long-term protection afforded by hepatitis A immunization and the development of diagnostic assays that can distinguish between vaccine-induced antibody and antibody produced in response to natural infection.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

The efficacy of HAVRIX was evaluated in a double-blind, placebo-controlled randomized clinical trial conducted in Thailand among approximately 40,000 children 1 to 16 years of age living in villages that had high rates of hepatitis A.

The efficacy of VAQTA was evaluated in a double-blind, placebo-controlled, randomized clinical trial among approximately 1,000 children 2 to 16 years of age living in a New York community that had a high rate of hepatitis A.

Several epidemiologic studies have evaluated the effectiveness of hepatitis A virus (HAV) vaccines in controlling outbreaks in communities with high or intermediate rates of hepatitis A.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Decreased incidence of hepatitis A virus (HAV) infections
- Eradication of hepatitis A

POTENTIAL HARMS

Hepatitis A virus (HAV) vaccines: Data concerning adverse effects of HAV vaccines, derived from pre-licensure clinical studies and post-licensure reports to

the national Vaccine Adverse Events Reporting System (VAERS), are summarized below:

- HAVRIX: Approximately 50,000 persons have been administered HAVRIX in clinical studies. No serious adverse events have been attributed definitively to hepatitis A vaccine. Among adults, the most frequently reported side effects occurring within 3 days after the 1,440 EL.U. dose were soreness at the injection site (56%), headache (14%), and malaise (7%); the incidence of side effects generally has been similar to that of hepatitis B vaccine. In clinical studies among children, the most frequently reported side effects were soreness at the injection site (15%), feeding problems (8%), headache (4%), and injection-site induration (4%). No serious adverse events were reported for approximately 40,000 children who were administered the 360 EL.U. dose of hepatitis A vaccine in a protective efficacy study.
- VAQTA: Approximately 9,200 persons have been administered VAQTA in clinical studies. No serious adverse events were reported among participants in the clinical studies. Among adults, the most frequent side effects that occurred within 5 days following vaccination include tenderness (53%), pain (51%), and warmth (17.3%) at the injection site (53%) and headache (16.1%). Among children, the most common side effects reported were pain (19%), tenderness (17%), and warmth (9%) at the injection site.

Immune globulin (IG): Serious adverse events from IG are rare. Anaphylaxis has been reported after repeated administration to persons who have known IgA deficiency; thus, IG should not be administered to these persons. IG may interfere with the response to live, attenuated vaccines (e.g., measles, mumps, rubella, and varicella) when vaccines are administered either individually or as combination vaccines.

Subgroups Most Likely to be Harmed:

Hepatitis A vaccine should not be administered to persons with a history of hypersensitivity to alum or, in the case of HAVRIX, to the preservative 2-phenoxyethanol.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Because of their critical role in hepatitis A virus (HAV) transmission, children should be a primary focus of immunization strategies to lower disease incidence. Because a vaccine formulation or schedule for vaccinating children during the first two years of life is not currently available, routine vaccination of older children is required to achieve effective prevention and control of this disease. Elimination of HAV transmission will become an attainable goal once hepatitis A vaccine can be used for infant and early childhood immunization.
- Before recommendations can be made concerning the possible need for booster doses, the long-term protective efficacy of hepatitis A vaccine is being monitored, as has been done for other vaccines, by collecting surveillance data and conducting population-based studies.

- Studies of chimpanzees indicate hepatitis A vaccine can prevent HAV infection if administered shortly after exposure. Clinical efficacy trials of hepatitis A vaccine suggest a possible postexposure effect. Results of an appropriately designed clinical trial comparing the postexposure efficacy of vaccine with that of immune globulin (IG) are needed to determine if hepatitis A vaccine without IG could be recommended to prevent hepatitis A after exposure.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1999 Oct 1;48(RR-12):1-37. [161 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Oct 1

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Hepatitis A Working Group Advisory Committee on Immunization Practices (ACIP)

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline. This report updates the ACIP's 1996 recommendations on the prevention of hepatitis A through immunization (MMWR 1996;45:[No. RR-15]).

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site.

Print copies: Available from the CDC, 1600 Clifton Rd, Atlanta, GA 30333 U.S.A

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 1, 1999. The information was verified by the guideline developer on April 10, 2000.

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Date Modified: 11/15/2004